



AI can now identify atrial fibrillation through sinus rhythm

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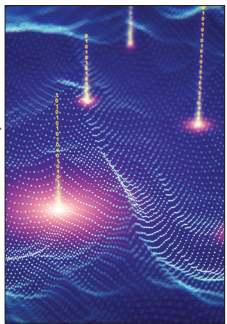
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- 1 Lammert F, Marschall HU, Glantz A, Matern S. Intrahepatic cholestasis of pregnancy: molecular pathogenesis, diagnosis and management. *J Hepatol* 2000; **33**: 1012–21.
- 2 Geenes V, Williamson C. Intrahepatic cholestasis of pregnancy. *World J Gastroenterol* 2009; **15**: 2049–66.
- 3 Glantz A, Marschall HU, Mattsson LA. Intrahepatic cholestasis of pregnancy: relationships between bile acid levels and fetal complication rates. *Hepatology* 2004; **40**: 467–74.
- 4 Ovadia C, Seed PT, Sklavounos A, et al. Association of adverse perinatal outcomes of intrahepatic cholestasis of pregnancy with biochemical markers: results of aggregate and individual patient data meta-analyses. *Lancet* 2019; **393**: 899–909.
- 5 Chappell LC, Gurung V, Seed PT, Chambers J, Williamson C, Thornton JG. Ursodeoxycholic acid versus placebo, and early term delivery versus expectant management, in women with intrahepatic cholestasis of pregnancy: semifactorial randomised clinical trial. *BMJ* 2012; **344**: e3799.
- 6 Gurung V, Middleton P, Milan SJ, Hague W, Thornton JG. Interventions for treating cholestasis in pregnancy. *Cochrane Database Syst Rev* 2013; **6**: CD000493.
- 7 Shen Y, Zhou J, Zhang S, et al. Is it necessary to perform the pharmacological interventions for intrahepatic cholestasis of pregnancy? A Bayesian network meta-analysis. *Clin Drug Investig* 2019; **39**: 15–26.
- 8 Chappell LC, Bell JL, Smith A, et al. Ursodeoxycholic acid versus placebo in women with intrahepatic cholestasis of pregnancy (PITCHES): a randomised controlled trial. *Lancet* 2019; published online Aug 1. [http://dx.doi.org/10.1016/S0140-6736\(19\)31270-X](http://dx.doi.org/10.1016/S0140-6736(19)31270-X).
- 9 Royal College of Obstetricians and Gynaecologists. Obstetric cholestasis: green-top guideline no. 43. London: Royal College of Obstetricians and Gynaecologists, 2011.



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Atrial fibrillation is a substantial health-care challenge and is considered to be a global pandemic, as prevalence rates have increased greatly¹ and atrial fibrillation-related hospitalisations outnumber those of major cardiac conditions such as heart failure and myocardial infarction.² Atrial fibrillation confers an increased risk of stroke and mortality; it therefore needs to be detected not only to manage the arrhythmia but also to prevent comorbidities and death.³ A 10-second, 12-lead electrocardiograph (ECG) in current clinical practice is unlikely to reveal possible atrial fibrillation if not present in this short monitoring time. Silent or undetected atrial fibrillation is common and the few screening methods available are demanding in terms of time and resources. Continuous monitoring by means of loop recorders is often indicated, particularly in case of embolic stroke of undetermined source (ESUS).⁴ Novel and user-friendly wearables to identify arrhythmias have emerged with recent digital advances: wearable ECG technology using automated photoplethysmography algorithms have shown feasible and accurate cardiac rhythm detection and can aid in monitoring the dynamic burden of time spent in atrial fibrillation,⁵ while mobile atrial fibrillation applications are available for patients and health-care professionals for education and guidance in management.⁶

In *The Lancet*, Zachi Attia and colleagues⁷ report a study in which they aimed to develop and validate an artificial intelligence (AI)-enabled ECG using a trained neural network to detect the electrocardiographic signature of atrial fibrillation during sinus rhythm.

Structural changes in the atria predispose to atrial arrhythmias.⁸ Deducing atrial fibrillation in a sinus rhythm ECG has been attempted previously by using P wave and PR interval traces to describe phenomena such as interatrial block.⁹ Here, Attia and colleagues hypothesised that the signature of atrial fibrillation due to the structural changes in the atria could be identified by a trained network, using a standard 10-second, 12-lead ECG recorded during sinus rhythm. Rather than trying to observe atrial fibrillation by prolonged monitoring of sinus rhythm, the authors suggest that AI can avoid this needle-in-a-haystack scenario and instead identify from as few as one normal sinus rhythm ECG if there is indeed a needle hidden within. P wave characteristics are likely to be picked up by the network, but no criteria are predefined or revealed in retrospect. In total, almost 650 000 ECGs from a cohort of 180 922 patients aged 18 years or older with at least one normal sinus rhythm, standard 10-second, 12-lead ECG from the Mayo Clinic ECG laboratory, were used to develop, test, and validate the network. Patients and their digitally available ECGs were randomly assigned to three datasets: a training dataset (70% of the patient cohort) used to train the network, an internal validation dataset (10% of the patient cohort) to optimise the network, and a testing dataset (20% of the patient cohort) to identify the ability of the AI-enabled ECG to detect atrial fibrillation. When using a single AI-enabled ECG, mathematical performance of the network showed an impressive area under the curve of the operating receiver curve of 0.87 (95% CI

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0.86–0.88), sensitivity of 79.0% (77.5–80.4), specificity of 79.5% (79.0–79.9), F1 score of 39.2% (95% CI 38.1–40.3), and overall accuracy of 79.4% (79.0–79.9). Performance improved when including all ECGs acquired during each patient's window of interest, which began at the study start date for those without atrial fibrillation and 31 days before the first recorded atrial fibrillation ECG for patients with atrial fibrillation.

There are several strengths of the approach taken by Attia and colleagues. First, they used a large cohort of patients and their ECGs and prevented bias by dividing the patients over three datasets, demonstrating a robust approach. Their findings will be of clinical importance, especially in identifying silent atrial fibrillation, and might have important implications for secondary prevention of patients with ESUS in terms of providing appropriate oral anticoagulation to prevent recurrences of stroke. Furthermore, this approach could lead to a paradigm shift in recording sinus rhythm rather than atrial fibrillation on an ECG, with a specific focus on identifying structural changes. However, false negatives might also be part of the outcomes and would prevent appropriate therapy. Moreover, the network has been tested to retrospectively identify atrial fibrillation rather than predicting atrial fibrillation. The AI-enabled algorithm would require further validation in a different patient cohort, testing a healthier out-of-hospital population, as well as a rigorous prospective clinical trial assessment. Advanced refinement might be necessary before the network can be used for primary atrial fibrillation prediction.

Notwithstanding the limitations, the network can support clinical decision making, helping to relieve the health-care burden related to atrial fibrillation. Further improvement of available systems, as well as related research, is warranted to optimise the identification of atrial fibrillation and appropriate management accordingly. Combining ECG algorithms with age, gender, clinical features, and biomarkers¹⁰ might further improve identification of patients with atrial fibrillation. Additionally, linking these variables with genetic markers,¹¹ AI-enabled algorithms,⁷ and smart monitoring by means of wearables⁵ to diagnose atrial fibrillation and quantify atrial fibrillation burden promises a safer and more efficient prevention of atrial fibrillation-related complications.

In summary, Attia and colleagues are to be congratulated for their innovative approach and the thorough development and local validation of the AI-enabled ECG. Given that AI algorithms have recently reached cardiologist level in diagnostic performance,¹² this AI-ECG interpretation is ground-breaking in creating an algorithm to reveal the likelihood of atrial fibrillation in ECGs showing sinus rhythm.

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- 1 Chugh SS, Havmoeller R, Narayanan K, et al. Worldwide epidemiology of atrial fibrillation: a Global Burden of Disease 2010 Study. *Circulation* 2014; **129**: 837–47.
- 2 Gallagher C, Hendriks JM, Giles L, et al. Increasing trends in hospitalisations due to atrial fibrillation in Australia from 1993 to 2013. *Heart* 2019; published online April 1. DOI:10.1136/heartjnl-2018-314471.
- 3 Kotecha D, Breithardt G, Camm AJ, et al. Integrating new approaches to atrial fibrillation management: the 6th AFNET/EHRA Consensus Conference. *Europace* 2018; **20**: 395–407.
- 4 Sanna T, Diener HC, Passman RS, et al. Cryptogenic stroke and underlying atrial fibrillation. *N Engl J Med* 2014; **370**: 2478–86.
- 5 Dorr M, Nothmann V, Brasier N, et al. The WATCH AF trial: smartwatches for detection of atrial fibrillation. *JACC Clin Electrophysiol* 2019; **5**: 199–208.
- 6 Kotecha D, Chua WWL, Fabritz L, et al. European Society of Cardiology smartphone and tablet applications for patients with atrial fibrillation and their health care providers. *Europace* 2018; **20**: 225–33.
- 7 Attia ZI, Noseworthy PA, Lopez-Jimenez F, et al. An artificial intelligence-enabled ECG algorithm for the identification of patients with atrial fibrillation during sinus rhythm: a retrospective analysis of outcome prediction. *Lancet* 2019; published online Aug 1. [http://dx.doi.org/10.1016/S0140-6736\(19\)31721-0](http://dx.doi.org/10.1016/S0140-6736(19)31721-0).
- 8 Kottkamp H. Human atrial fibrillation substrate: towards a specific fibrotic atrial cardiomyopathy. *Eur Heart J* 2013; **34**: 2731–38.
- 9 Martinez-Selles M, Masso-van Roessel A, Alvarez-Garcia J, et al. Interatrial block and atrial arrhythmias in centenarians: prevalence, associations, and clinical implications. *Heart Rhythm* 2016; **13**: 645–51.
- 10 Chua W, Purmah Y, Cardoso VR, et al. Data-driven discovery and validation of circulating blood-based biomarkers associated with prevalent atrial fibrillation. *Eur Heart J* 2019; **40**: 1268–76.
- 11 Roselli C, Chaffin MD, Weng LC, et al. Multi-ethnic genome-wide association study for atrial fibrillation. *Nat Genet* 2018; **50**: 1225–33.
- 12 Hannun AY, Rajpurkar P, Haghighpanahi M, et al. Cardiologist-level arrhythmia detection and classification in ambulatory electrocardiograms using a deep neural network. *Nat Med* 2019; **25**: 65–69.